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09/939,518	08/24/2001	Mark J. Jaroszeski	93004	2429

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EXAMINER

ANGELL, JON E

ART UNIT PAPER NUMBER

1635

DATE MAILED: 12/17/2002

Please find below and/or attached an Office communication concerning this application or proceeding.



Art Unit: 1635

### **DETAILED ACTION**

1. This Action is in response to the communication filed on 10/9/02, as Paper No. 10. Claims 2, 5, 11, 12, 15, 18 and 20 have been amended. Claims 3, 9, 13 and 19 have been cancelled. Claims 1, 2, 4-8, 10-12, 14-18 and 20 are pending in the application and are examined herein.
2. Applicant's arguments are addressed on a per section basis. The text of those sections of Title 35, U.S. Code not included in this Action can be found in a prior Office Action. Any rejections not reiterated in this action have been withdrawn as being obviated by the amendment of the claims and/or applicant's arguments.

#### ***Declaration under 37 CFR 1.132***

The Declaration filed under 37 CFR 1.132 is deemed to be insufficient.

The Declaration indicates, "Applicant herein declares that the above mentioned references are Applicant's own work which Applicant invented and reduced to practice prior to publication date of the reference." The declaration is signed by one Applicant (Jaroszeski). This is not sufficient because: 1) The other applicants (Heller and Gilbert) are not recognized as inventors in the 1.132 Declaration, but are authors in both cited references and are listed as inventors in the application; and 2) There is no specific statement in the declaration indicating that the other authors of the references (i.e. Lucas, Heller, Schultz, et al.) were merely working under direction of the applicant (see MPEP 715.02). Therefore, the declaration is insufficient to overcome the cited references, and the rejections stand for the reasons of record.

***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 2 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

5. The instant claims are drawn to a method/system for delivering a molecule into a target tissue comprising administration of a low level electric field for “a duration of at least 100m seconds”. This phrase constitutes new matter because there is now no upper limit to the duration of time for which the electric field can be applied. Therefore, the claims encompass applying an electric field for a duration of at least 100ms up to infinity. The specification discloses, “the duration of the pulse ranges from 0.1s to 20 minutes, with 100ms to 100 s duration comprising a preferred range” (see p. 6 lines6-9); indicating that duration of the electric pulse can be no longer than 20 minutes. Therefore, claims 2 and 12 are rejected for containing new matter.

***Claim Rejections - 35 USC § 102***

1. Claims 1, 4-8, 10, 11, 14-18 and 20 stand rejected under 35 U.S.C. 102(a) as being anticipated by Lucas et al. (DNA and Cell Biol. Vol. 20(3):183-8; March 2001).

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***Response to Arguments***

2. Applicant's arguments filed 10/9/02 have been fully considered but they are not persuasive. Applicants argue that that the instant rejection is traversed under 37 CFR 1.132 and accordingly, Lucas is not prior art.

3. In response, it is noted that the declaration submitted under 37 CFR 1.132 is insufficient to overcome the rejection for the reasons set forth above. Therefore, the reference is considered prior art and the rejection stands for the reasons of record as there are no other arguments against the rejection.

4. Claims 1, 4-5 and 14, and 16-18 and 20 are rejected under 35 U.S.C. 102(a) as being anticipated by Heller et al. (DNA and Cell Biol. Vol. 20(1):21-6; January 2001).

***Response to Arguments***

5. Applicant's arguments filed 10/9/02 have been fully considered but they are not persuasive. Applicants argue that that the instant rejection is traversed under 37 CFR 1.132 and accordingly, Lucas is not prior art.

6. In response, it is noted that the declaration submitted under 37 CFR 1.132 is insufficient to overcome the rejection for the reasons set forth above. Therefore, the reference is considered prior art and the rejection stands for the reasons of record as there are no other arguments against the rejection.

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7. Claims 1, 4-5 and 14, 15 and 16-19 and 20 stand rejected under 35 U.S.C. 102(a) as being anticipated by Bettan et al. (Bioelectrochemistry Vol. 52:83-90; September 2000) for the reasons of record set forth in the previous Office Action.

*Response to Arguments*

8. Applicant's arguments filed 10/9/02 have been fully considered but they are not persuasive.

9. Applicants assert that Bettan describes submitting each tumor to eight pulses of 20ms duration at a voltage-distance ratio ranging from 200 to 800V/cm, which applicants contend is a series of low-level pulses to affect the delivery of the molecules into the target tissue—different from the claimed substantially continuous low-level electric field which is not a series of pulses.

In response, it is respectfully pointed out that the claims are drawn to a method/system of facilitating the delivery of a molecule into a target tissue comprising applying “a substantially continuous low-level electric field to the target tissue for a duration sufficient... to facilitate entry of a desired molecule into an interior of the cell.” It is noted that the claims do not set forth the parameters which define the “substantially continuous low-level electric field”. Turning to the specification for guidance, it is clear that the specification discloses, “The characteristics of the field used to facilitate the entry of the molecules into the target cell include field strengths between 1mV/cm and 200V/cm, applied as pulses of substantially continuous energy. The duration of the pulse ranges from 0.1s to 20 minutes, with 100ms to 100s duration comprising a preferred range. A single pulse may be applied or a plurality of sequential pulses...” (see page 6 lines 5-12); thus defining the parameters of a substantially continuous field which would facilitate entry into a target cell when applied as any single pulse in the range of 1mV/cm and

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200V/cm and for a duration of 0.1s to 20 minutes (with 100ms to 100s duration comprising a preferred range). Therefore, any electric pulse within these parameters would inherently have the same effect and result in the desired outcome.

Bettan teaches that the electric field is 200V/cm for 20 to 50ms, within the range defined by the specification as able to facilitate porosity of a target cells and facilitate entry of a molecule into said cell. Therefore, a single pulse of the method taught by Bettan would inherently result in entry of a molecule into the cell, regardless if multiple pulses were applied..

10. Claims 1, 4-6, 8-11, 14-16, 18 and 20 stand rejected under 35 U.S.C. 102(b) as being anticipated by Mir et al. (PNAS Vol. 96:4262-4267; April 1999) for the reasons set forth in the previous Office Action.

#### ***Response to Arguments***

11. Applicant's arguments filed 10/9/02 have been fully considered but they are not persuasive.

12. Applicants assert that Mir describes a method comprising application of a series of low-level pulses to affect the delivery of the molecules into the target tissue—different from the claimed substantially continuous low-level electric field, which is not a series of pulses.

In response, it is respectfully pointed out that the claims are drawn to a method/system of facilitating the delivery of a molecule into a target tissue comprising applying “a substantially continuous low-level electric field to the target tissue for a duration sufficient... to facilitate entry of a desired molecule into an interior of the cell.” It is noted that the claims do not set forth



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the parameters which define the “substantially continuous low-level electric field”. Turning to the specification for guidance, it is clear that the specification discloses, “The characteristics of the field used to facilitate the entry of the molecules into the target cell include field strengths between 1mV/cm and 200V/cm, applied as pulses of substantially continuous energy. The duration of the pulse ranges from 0.1s to 20 minutes, with 100ms to 100s duration comprising a preferred range. A single pulse may be applied or a plurality of sequential pulses...” (see page 6 lines 5-12); thus defining the parameters of a substantially continuous field which would facilitate entry into a target cell when applied as any single pulse in the range of 1mV/cm and 200V/cm and for a duration of 0.1s to 20 minutes (with 100ms to 100s duration comprising a preferred range). Therefore, any electric pulse within these parameters would inherently have the same effect and result in the desired outcome.

Mir teaches that the electric field can be 100V/cm, but was optimal at 200V/cm for 20ms, which is within the range defined by the specification as able to facilitate porosity of a target cells and facilitate entry of a molecule into said cell. Therefore, a single pulse of the method taught by Mir would inherently result in entry of a molecule into the cell, regardless if multiple pulses were applied..

13. Claims 1-20 stand rejected under 35 U.S.C. 102(b) as being anticipated by Hofmann et al. (U.S. Patent 6,055,453, published April 25, 2000), for the reasons of record.

***Response to Arguments***

14. Applicant's arguments filed 10/9/02 have been fully considered but they are not persuasive.

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15. Applicants assert that Hofmann describes a method comprising application of a series of low-level pulses to affect the delivery of the molecules into the target tissue—different from the claimed substantially continuous low-level electric field, which is not a series of pulses.

In response, it is respectfully pointed out that the claims are drawn to a method/system of facilitating the delivery of a molecule into a target tissue comprising applying “a substantially continuous low-level electric field to the target tissue for a duration sufficient... to facilitate entry of a desired molecule into an interior of the cell.” It is noted that the claims do not set forth the parameters which define the “substantially continuous low-level electric field”. Turning to the specification for guidance, it is clear that the specification discloses, “The characteristics of the field used to facilitate the entry of the molecules into the target cell include field strengths between 1mV/cm and 200V/cm, applied as pulses of substantially continuous energy. The duration of the pulse ranges from 0.1s to 20 minutes, with 100ms to 100s duration comprising a preferred range. A single pulse may be applied or a plurality of sequential pulses...” (see page 6 lines 5-12); thus defining the parameters of a substantially continuous field which would facilitate entry into a target cell when applied as any single pulse in the range of 1mV/cm and 200V/cm and for a duration of 0.1s to 20 minutes (with 100ms to 100s duration comprising a preferred range). Therefore, any electric pulse within these parameters would inherently have the same effect and result in the desired outcome.

Hoffman teaches that the electric field strength can be from about 10V/cm to about 20kV/cm and the pulse length can be about 10us to about 100ms, which is within the range defined by the specification as able to facilitate porosity of a target cells and facilitate entry of a

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molecule into said cell. Therefore, a single pulse of the method taught by Hoffman would inherently result in entry of a molecule into the cell, regardless if multiple pulses were applied.

*Conclusion*

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to J. Eric Angell whose telephone number is (703) 605-1165. The examiner can normally be reached on M-F (8:00-4:30).

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader can be reached on (703) 308-0447. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

J. Eric Angell  
December 16, 2002

  
DAVE T. NGUYEN  
PRIMARY EXAMINER